



IJPPR

INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals

ISSN 2349-7203



Human Journals

Review Article

August 2021 Vol.:22, Issue:1

© All rights are reserved by Amit Chaudhary et al.

The Potential and Outgoing Trends in Traditional, Phytochemical, and Ethnopharmacological Activity of *Gentiana olivieri*: A Comprehensive Review



IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals

ISSN 2349-7203



Nitin Chandel¹, Amit Chaudhary^{1*}, Diksha Choudhary¹, Kapil Kumar Verma²

¹ School of Pharmacy, Abhilashi University, Chail Chowk, Mandi, Himachal Pradesh-175028 India.

² Minerva College of Pharmacy, Indora, Kangra, Himachal Pradesh-176402 India.

Submitted: 23 July 2021
Accepted: 29 July 2021
Published: 30 August 2021



HUMAN JOURNALS

www.ijppr.humanjournals.com

Keywords: Potential and Outgoing Trends, Traditional, Phytochemical, and Ethnopharmacological Activity, *Gentiana olivieri*

ABSTRACT

Gentiana, a cosmopolitan and important genus of the Gentianaceae family, comprises 400 species distributed among the world. Based on the studies of Iranian traditional medicine texts, there are some promising bioactivities for this genus that are unknown in modern medicine and some of them are still the basis of new remedies. Whole plant of *Gentiana olivieri* Griseb. holds a rich source of secondary metabolites including alkaloids, bitter secoiridoid glycosides, triterpenes, fats, flavone-c-glycosides (isoorientin). The alkaloids (gentianine, gentianidine) have been culpable for their manifold pharmacological activities such as antibacterial, antifungal, hypotensive and the flavone-c-glycosides (isoorientin) have been responsible for the anti-inflammatory, anti-nociceptive, gastroprotective, hepatoprotective, antidiabetic effect. In this review, an attempt has been made to enlightened morphology, phytochemistry, ethnobotanical and reported pharmacological activities in the last six years for exploring the interminable medicinal potential of *Gentiana olivieri*.

INTRODUCTION

Indian Ayurveda along with the Siddha, Jammu, Tibetan, Traditional Chinese, and Unani systems of medicine are an essential source of health and livelihood for millions of Asian people. Ayurvedic medicine is broadly practiced particularly in Bangladesh, India, Nepal, Pakistan, and Sri Lanka^[1]. Gentianaceae is an ethnobotanically important family used extensively in Unani, Ayurvedic and Chinese traditional medicine systems. Famous Unani formulations (Tiryaaq Samania, Tiryaaq Arbaa) employed the use of plants from this precious family ^[2]. The angiosperms family Gentianaceae is comprised of 87 genera and 1615–1688 species and has been celestially accepted in all subsequent considerable classifications. It is a family that appears great adaption in habit, morphology, anatomy, geographical distribution. The plants of the family are annual and perennial herbs or shrubs ^[3]. Plants belonging to genus *Gentiana* are very well-known for their ethnomedicinal and phytopharmacological action. People living in the mountains of Pakistan use *Gentiana* in many ways such as medicines, timber wood, firewood, food, fodder etc. *Gentiana* is comprised of intensely bitter glycosides^[5] which have been responsible for its immense therapeutic potential. Recently interest in this potent medicinal plant has been revived and various significant phytoconstituents like olivierosides, oliveramine, gentianine, isoorientin, gentianamine etc. have been studied for drug development and discovery. ^[6-7]

Gentiana olivieri Griseb. (Afat), belonging to the Gentianaceae family ^[8] is widely used as a bitter tonic, stomachic, appetizer, antipyretic, anticonvulsant, antidiabetic, antihepatotoxic, antinociceptive, anti-inflammatory, antiulcerogenic, sedative, antioxidant, antidepressant, and antianemic ^[9]. The plant is known to possess several bitter secoiridoids glycosides, flavonoids (isoorientin and its derivatives), alkaloids, xanthones, triterpenoid acids, and fats ^[10]. Recently, among the species of the Gentianaceae family, *G. olivieri* has been a focus of interest due to the identification of phytochemicals such as amarogentin and sweroside as new potential drugs ^[9-12].

Vernacular Names ^[13]

Unani: Gul-e-ghafis, English: Gentian, Hindi: Asbarg, Pakistan: Bangera, Turkey: Afat

Taxonomic Classification [14-15]

Kingdom	:	<i>Plantae</i>
Division	:	<i>Magnoliophyta</i>
Class	:	<i>Magnoliopsida</i>
Subclass	:	<i>Asteridae</i>
Order	:	<i>Gentianales</i>
Family	:	<i>Gentianaceae</i>
Genus	:	<i>Gentiana</i>
Species	:	<i>Olivieri</i>

Plant Description

Gentiana olivieri Griseb. perennial herbaceous plant 10–40 cm tall grows at an altitude of 350–2300 meters. Linear- elliptic to elliptic-lanceolate, narrowed leaf with acuminate apex and distinct veins. The perennial stem is erect, slender and glabrous. Flowers (3–5) are arranged in terminal corymbose cymes inflorescences. Pedicel is 3 to 5 cm, calyx tube (4–8 mm) is obconic; lobes are triangular, unequal. Corolla is blue colored with obconic lobes having entire margin. Stamens are inserted just below middle of corolla tube; filaments are 6–8 mm; long with linear anthers. Capsules type seeds (0.8–1 mm) are brown, ellipsoid with thick reticulate seed coat [16–17].

Habitat

Gentiana olivieri Griseb. is abundantly found in Temperate and Tropical Asia including regions of Western Asia, Middle Asia, Indian subcontinent, Afghanistan, Pakistan, Iran, Iraq, Syria, Turkey, Armenia. The plant is also found in the temperate region of Gulf countries and some temperate regions of China[18].

Traditional Uses

Gentiana olivieri is used in traditional medicine in Unani and Ayurveda system of medicines

in arthritis, anti-inflammatory, antidepressant, antiulcerogenic, gastro-protectant and sudorific^[15,19]. It has been employed as a hepatoprotective, aphrodisiac plant in Turkey^[20–21]. In the Uzbekistan Republic, it has been used as ailment of common cold, indigestion, diarrhea, stomachache^[22]. Decoction of root is used for urinary tract infections in Pakistan^[23]. *Kabdeen* a famous unani antiviral formulation involves use of extract of *Gul-e-ghafis* i.e. *Gentiana olivieri* Griseb^[24].

Based on the Iranian traditional medicine texts *Gentiana*'s species have different therapeutic properties which are related to the root of the plant. Treatment of urinary retention, menstrual, liver and spleen dysfunctions and detoxifying of animal poisons are the main and common properties among the texts ^[25-27].

Phytochemistry of *Gentiana olivieri* Griseb.

Gentiana olivieri Griseb. contain major class of secondary metabolites are alkaloids, glycosides, flavonoids, triterpenoids, fats etc. From the ethanolic extract of whole plant of *Gentiana olivieri* Griseb. two alkaloids gentianine and gentianidine have been isolated using silica gel column chromatography eluting with chloroform:hexane (20:1)^[28] and different saturated pentadecanoic, hexadecanoic, heptadecanoic, octadecanoic, nonadecanoic along with a unsaturated fatty acid hepta-decatrienoic acid have also been isolated when eluted with hexane:ether (1:3). Methanolic extract also provides three new bitter secoiridoid glycosides, olivierosides A, B and C together with known compounds, gentiopicroside, swero-side, 6'-O- β -D-glucosylgentiopicroside, swertiapunimarin, eustomoside, eustomorusside and septemfidoside^[29]. The flowers of *Gentiana olivieri* Griseb. also afforded oleanolic and ursolic acids^[19]. The ethyl acetate fraction of ethanolic extract of *Gentiana olivieri* Griseb. when subjected to silica gel column chromatography gave flavone-c-glycosides (C-glycosylflavone) – Isoorientin^[30-31]. Aerial parts of *Gentiana olivieri* Griseb. provides alkaloids – gentiana- mine, gentianidine, gentianine, gentioflavin, oliverine, olivieridine, gentiotibetine, olvieramine. The structures have been established on the basis of chemical evidence and spectroscopic methods^[32–35].

A new depside, olivieridepside, and a new secoiridoid, olivierigenin were isolated from the aerial parts of *Gentiana olivieri* Griseb. along with four known compounds, gentiopicroside, olivierosides A and B and isoorientin. The structures of the isolates were determined by

extensive 1D and 2D NMR spectroscopy and HR-MS analysis. This is the first report on the occurrence of a depside structure in the genus *Gentiana*. Moreover, a rare type of non-glycosidic secoiridoid (2) lacking an oxygenated group at C-1 is also being reported for the first time from this genus [36].

Reported Activity

Various extracts of *Gentiana olivieri* Griseb. were evaluated for screening *in-vitro/ in-vivo* pharmacological models. Isoorientin isolated from the ethyl acetate fraction of ethanolic extract exhibited significant hypoglycemic, antihyperlipidemic^[30] hepatoprotective^[31], anti-inflammatory, anti-nociceptive, gastroprotective effects^[37]. Furthermore, Gentianine (alkaloid) isolated from ethanolic extract of the whole plant of *Gentiana olivieri* Griseb. showed significant antibacterial, antifungal activity^[38] along with hypotensive effects [38–39]. Activities reported in past six years are given below.

Appetizing Effect

A case-control study was performed in which the plant's root extract was used to prepare hydroalcoholic product (2.5%) and its appetizing effect was evaluated in children. Fifty children with anorexia were randomly divided into two groups to receive either the hydroalcoholic extract of the *Gentiana olivieri* or a placebo at the dose of 2.5 mg/kg/day for two months. Variables such as weight, height, waist, consumed calories, and hunger VAS score, liver enzymes fluctuations and some blood biochemistry tests were also monitored. The average age of cases and controls was 56.12 and 56.64 months, respectively. Before treatment, the mean weight in both case and control groups was 13.130±1.56 kg and 13.010±1.27 kg, respectively that changed to 14.275 ± 1.69 kg and 12.962± 1.16 kg after a month and 14.550±1.54 kg and 12.814±1.22 kg, respectively two months after the intervention. Significant effects were seen on received calories and VAS score. The product was found to have a significant effect on weight, food intake and VAS score compared with placebo [40].

The roots of *Gentiana olivieri* (Gentianaceae), an Iranian indigenous plant, were studied to standardize and prepare an appetite-stimulating drug. The bitterness value of the aqueous extract of the plant was evaluated for its efficacy as an appetite-stimulant. It was found to be very bitter, with a bitterness value of 33,183.5, which is comparable to the value reported for

the internationally well-known bitter plant, *Gentiana lutea* L. To standardize *G. olivieri* to prepare an appetite-enhancing drug, separation of the bitter compound gentiopicroside from the plant *G. lutea* was carried out by using Prep TLC. The extracted pure compound was identified by the FTIR method, gas chromatography, mass spectrometry, and HPLC, and then used as a standard for later quantitative research. The *G. olivieri* extract was standardized based on the amount of gentiopicroside as an effective component. To formulate appetite-stimulating medicine, the extraction of the plant was conducted according to the methods mentioned in the British Pharmacopoeia. Then, a hydroalcoholic solution of the plant extract was formulated. The microbiological control of the plant extract and herbal medicine were investigated. The results showed no microbial growth within 30 days. The amount of gentiopicroside obtained from the hydroethanolic extract of the *G. olivieri* was 586.6 ppm. Furthermore, the bitterness value of the plant exceeded the amount mentioned in the pharmacopoeia for the hydroethanolic extract of *G. lutea*. Therefore, it can be implied that the effect of this natural medicine will be to increase appetite [41].

Antidepressant Activity

The antidepressant effect of *G. olivieri* ethanol extract (GOEE) in a chronic mild stress-induced rat model, which was used to mimic a depressive state in humans, and to compare the effect with that of imipramine. Male Sprague-Dawley rats were randomly divided into six groups: control, stress, treated with imipramine (positive control), and treated with GOEE at three different (200, 500, 1000 mg/kg) doses groups. The rats in all groups, except the control group, were exposed to chronic mild stress. At the end of the 3-week experimental period, biochemical and behavioral parameters were examined. The results showed that treatment with GOEE or imipramine significantly improved rats' sucrose consumption which was diminished by chronic mild stress, restored serum levels of corticosterone and proinflammatory cytokines (interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α)), prevented the increase of liver index of rats. Moreover, in the hippocampus tissue, decreased serotonin and noradrenaline levels were significantly increased by treatment with GOEE or imipramine, and antioxidant parameters (thiobarbituric acid reactive substances (TBARS), superoxide dismutase (SOD), and glutathione (GSH)) were significantly improved by treatment with GOEE though not with imipramine. The data demonstrate that *G. olivieri* may exert its antidepressant activity by improving monoaminergic system disorders, and by favorably affecting the antioxidant, inflammatory and endocrine mechanisms [42].

REFERENCES

1. WHO, Legal Status of Traditional Medicine and Complementary/ Alternative Medicine: A Worldwide Review; 2001WHO/EDM/TRM/2001.2, WHO, Geneva, p.188.
2. Kabi Hifzul. Morakkabat (Unani Formulations) Shamsher Publisher and Distributors Dist. Aligarh UP; 2003;India.
3. Daniel M, Sabnis SD. Chemical systematics of family Gentianaceae. Current Science. 1978;47:109–11.
4. Hostettmann-Kaldas M. Flavones and secoiridoids of American *Gentiana* species. Phytochemistry. 1981;20:443–46.
5. Brahamchari G. Swertia (Gentianaceae): Chemical and pharmacological aspects. Chemical Biodiversity. 2004;1:1627–51.
6. Mansoor A, Zaidi IM, Hayder M, Rasheed A. Antihypertensive effect of *Gentiana olivieri*. Journal of Medical Science, 2004;4(3):176–178.
7. Struwe L, Albert VA. Gentianaceae Systematics and Natural History. Cambridge University Press. 2002;1:22–24.
8. Orhan DD, Aslan M, Aktay G, Ergun E, Yesilada E, Ergun F. Evaluation of hepatoprotective effect of *Gentiana olivieri* herbs on subacute administration and isolation of active principle. Life Sciences. 2003 Apr 4;72(20):2273-83.
9. Prathapa Reddy M, Kavaya B, Rama Rao V, Shantha TR. Therapeutic uses of Flowers-Leads from Traditional System of Medicine.
10. Singh S, Yadav CP, Noolvi MN. Immunomodulatory activity of butanol fraction of *Gentiana olivieri* Griseb. on Balb/C mice. Asian Pacific journal of tropical biomedicine. 2012 Jun 1;2(6):433-7.
11. Peng J, Fan G, Hong Z, Chai Y, Wu Y. Preparative separation of isovitexin and isoorientin from *Patrinia villosa* Juss by high-speed counter-current chromatography. Journal of Chromatography A. 2005 May 13;1074(1-2):111-5.
12. Wang D, Xu M, Zhu HT, Chen KK, Zhang YJ, Yang CR. Biotransformation of gentiopicoside by asexual mycelia of *Cordyceps sinensis*. Bioorganic & medicinal chemistry letters. 2007 Jun 1;17(11):3195-7.
13. <http://en.wikipedia.org/wiki/Gentiana>.
14. Struwe L, Albert VA. *Gentianaceae Systematics and Natural History*. Cambridge University Press. 2002;1:22–24.
15. Kirtikar KR, Basu BD. Indian medicinal plants. Lalit Mohan Basu Allahabad, India. III Edition. 1998; p.1663.
16. Zheng W, Raven PH. Flora of China (<http://www.efloras.org>). 1994.
17. Tuzan CY, Toker MC, Toker G. Anatomical investigations on root, stem, and leaf of *Gentiana olivieri*. Pharmacogn Mag. 2011;7(25): 9–13.
18. McGuffin M, Kartesz J.T, Leung A.Y, Tucker A.O. (2000). Herbs of Commerce. 2nd ed. Silver Spring (MD): The American Herbal Products Association.
19. Chopra R.N, Nayar S.L, Chopra I.C. (2006). Glossary of Indian medicinal plants. NISCAIR Delhi: p.324–325.
20. Aktay G, Deliorman D, Ergun E, Ergun F, Yesilada E, Cevik C. Hepatoprotective effects of Turkish folk remedies on experimental liver injury. J Ethnopharmacol. 2000;73(1–2): 121–9.
21. Ozturk F, Olcuc C. Ethnobotanical features of some plants in the district of şemdinli (hakkari – turkey). International journal of academic research. 2011;3(1): 20–9.
22. Honda G. Kyoto: Kyoto University; 1999. A report on traditional medicine of Turkish people, (1997, 1998).
23. Ali H, Quaisar M. The ethnobotany of Chitral valley, Pakistan with particular reference to medicinal plants. Pak J Bot, 2009;41(4): 2009–2041.
24. Siddiqui MMH, Sultana A, Siddiqui MY. Effect of Kabdeem in warm-e- kabid vairoosi (viral hepatitis). IJTK, 2005;4(4): 416–420.
25. Aghilialavi H. Makhzan Al Advieh. Tehran: Sabzarang; 2008.
26. Momen Tonekaboni S. Tohfat Al-Momenin. Tehran, Iran: Shahr Publication; 2008:274.
27. Ansari A. Ekhtiarate Badiei. Tehran: Pakhshe Razi; 1992:99.
28. Mansoor A. Toxicological evaluation of the extract and pure compounds of *Gentiana olivieri*. Pakistan

Journal of Biological Sciences. 2003;6(23):1949–1950.

29. Takeda Y, Masuda T, Honda G, Takaishi Y, Ashurmetov M. (Secoiridoid Glycosides from *Gentiana olivieri*. Chemistry Pharma Bulletin, 1999;47(9):1338–1340.
30. Sezik E, Aslana M, Yesilada E, Itob S). Hypoglycaemic activity of *Gentiana olivieri* and isolation of the active constituent through bioassay- directed fractionation techniques. Life Sciences, 2005;76:1223–1238.
31. Orhana DD, Aslana M, Aktayb G, Ergunc E, Yesilada E, Erguna F. Evaluation of Hepatoprotective effect of *Gentiana olivieri* herbs on subacute administration and isolation of active principle. Life Sciences. 2003;72: 2273–2283.
32. Rakhmatullaev TU, Akramov ST, Yunusov SY, Soedinenii PK. Alkaloids of Gentiana. Structure of gentianadine and gentianamine, 1967;3(2): 182–187.
33. Rakhmatullaev TU, Akramov ST, Yunusov SY, Soedinenii PK. The alkaloids of *Gentiana olivieri*, 1969;5(6):608–13.
34. Rakhmatullaev TU, Yunusov SY. The alkaloids of *Gentiana olivieri*. The chemistry of plant substances, 1972;3:350–353.
35. Rakhmatullaev TU, Yunusov SY. The alkaloids of *Gentiana olivieri*. The chemistry of plant substance. 1973;1:64–67.
36. Kırmızıbekmez H, Tatar D, Erdoğan M, Kúsz N, Hohmann J. A new depside and a new secoiridoid from the aerial parts of *Gentiana olivieri* from flora of Turkey. Natural Product Research. 2020 Sep 24:1-7.
37. Kupeli E, Gurbuz I, Yesilada E. Evaluation of *in vivo* Biological Activity Profile of Isoorientin. Journal of Biochemical Sciences, 2004;59c: 787–790.
38. Mansoor A, Samad A, Zaidi MI, Aftab K. Hypotensive Effect of *Gentiana olivieri* and Its Alkaloid Gentianine in Rats. Pharmacy and Pharmacology Communications, 1998;4:229–230.
39. Mansoor A, Zaidi IM, Malghani MAK. Biological efficacy of the extract and pure compound of *Gentiana olivieri*. Pakistan Journal of Biological Sciences, 1999;2(3):807–808.
40. Nayebi E, Azadbakht M, Zamanfar D, Karami H, Enayati Fard R, Jafari Kokhdan A, Yazdani Cherati J. Appetizing effect of *Gentiana olivieri* extract in children with anorexia. Journal of Mazandaran University of Medical Sciences. 2016 Feb 10;25(133):58-66.
41. Azadbakht M, Nayebi E, Fard RE, Khaleghi F. Standardization and formulation of an herbal appetite-stimulating drug from *Gentiana olivieri*. Journal of Herbal Medicine. 2020 Feb 1;19:100306.
42. Berk A, Yılmaz İ, Abacıoğlu N, Kaymaz MB, Karaaslan MG, Kuyumcu Savan E. Antidepressant effect of *Gentiana olivieri* Griseb. in male rats exposed to chronic mild stress. Libyan Journal of Medicine. 2020 Jan 1;15(1):1725991.